Bipolar Disorder in Pregnancy

Background
1. Definition
   o Bipolar disorder occurring in a pregnant pt
2. General information
   o Early dx and obstetric care is key to maximizing health of mother and fetus

Pathophysiology
1. See Bipolar Disorder
2. Lifetime incidence
   o Psychosis affects 1 in 600 pregnant women
3. Lifetime prevalence in women
   o Bipolar I: 0.9%
   o Bipolar II: 0.5%
4. Risk factors
   o Bipolar affective puerperal psychosis (severe postpartum psychosis), is clustered in families, linked to chromosome 16p13
5. Morbidity/ mortality
   o Premature delivery
     ▪ Odds ratio: 1.40 vs normal controls
   o SGA infants
     ▪ Odds ratio: 1.39 vs normal controls
   o Manic episode incr risk for alcohol/ drug consumption, incr risk to fetus
   o Lithium, valproate, carbamazepine teratogenic in first trimester (Class D)
   o Antidepressant use w/o concomitant anti-manic medication incr risk for mania and accelerated cycling
   o Manic/ depressive/ psychotic episodes follow 25-50% of deliveries
     ▪ Highest risk in first pregnancy or pts w/prior severe postpartum relapses

Diagnostics
1. Diagnostic criteria
   o See Bipolar Disorder
2. Physical exam
   o Examine for medication SE (extrapyramidal symptoms)
     ▪ Tardive dyskinesia
     ▪ Resting tremor
     ▪ Akinesia
     ▪ Akathisia
     ▪ Dystonia
     ▪ "Lead pipe" rigidity
     ▪ Postural instability
   o Mania S/S
     ▪ Euphoria/ irritability
     ▪ Decr need for sleep
     ▪ Talkativeness
     ▪ Racing thoughts
     ▪ Hypersexuality
• Aggression
• Agitation
• Poor judgment
  o Depression S/S
    • Insomnia/ early morning awakening
    • Decr interest
    • Guilt/ feelings of worthlessness
    • Fatigue
    • Poor concentration
    • Reduced appetite/ wt loss
    • Suicidal ideation
    • Hy nexuality
3. Diagnostic testing
  o Lithium level
    • Every 2-4 wks in pregnancy
    • Weekly in last month
    • Every 2-3 days before and after delivery
  o Check Thyroid function tests
    • 1-2 times during initial 6 mos of lithium tx
    • q6-12 mos in pts chronically tx w/lithium
    • When changes in S/S or side effects occur
4. Diagnostic imaging
  o High-resolution ultrasound at 16-18 wks to detect cardiac defects if treated w/lithium, valproate, or carbamazepine
5. Other studies
  o If treated w/lithium, valproate, or carbamazepine
    • Maternal serum AFP screen for neural tube defects before wk 20
    • Amniocentesis and sonography if elevated AFP

Differential Diagnosis
1. Major depressive disorder
2. Dysthymic disorder
3. Bipolar I disorder
4. Bipolar II disorder
5. Cyclothymic disorder
6. Bipolar disorder NOS
7. Post partum depression

Therapeutics
1. Acute tx
  o ECT indicated for pregnant pts w/severe mania or depression
    • May present less fetal risk than other medical tx
  o First generation high potency antipsychotics
    • ex: Haloperidol
  o Benzodiazepines
    • Lorazepam is preferred if necessary for tx of acute agitation
2. Further mgmt (24 hrs)
   - Pre-conception or 1st trimester
     - Taper off medication if mild/moderate illness and avoid medication until at least second trimester
       - Close follow up is necessary to monitor for signs of relapse
   - Continue tx in pts that present for obstetric care in second or third trimester
   - High-potency first generation antipsychotic medications preferred especially in first trimester
     - Fluphenazine
     - Haloperidol
     - Perphenazine
     - Thiothixene
     - Trifluoperazine

3. Long-term care
   - Inform pt of high risk of postpartum relapse
   - Resume pre-pregnancy tx/dose (lithium/valproate) after delivery
   - Maintain normal sleep pattern postpartum to protect against manic episodes

4. Anti-manic agents
   - Lamotrigine
     - Pregnancy Category C
     - No documented incr in congenital anomalies
   - Typical antipsychotics
     - Pregnancy Category C
     - Not associated w/fetal anomalies
     - Haloperidol
     - Trifluoperazine
     - Perphenazine
     - Prochlorperazine
   - Atypical antipsychotics
     - Pregnancy Category C
     - Limited studies on teratogenicity
     - Monitor for wt gain, impaired glucose tolerance, and worsening lipid profile
     - Risperidone
     - Quetiapine
     - Olanzapine
     - Aripiprazole
   - Verapamil
     - Pregnancy Category C
     - Recommended for pts who respond to Lithium but cannot tolerate SE
     - Lack of teratogenicity supports use in pregnant bipolar pt
   - Lithium
     - Pregnancy Category D
     - Only mood stabilizer proven to reduce suicide in bipolar pts
     - Discontinue lithium during first trimester: weigh risks vs. benefits
     - Rate of relapse is incr by lithium discontinuation, especially if stopped abruptly
- Absolute risk for Ebstein's anomaly:
  - 1-2 per 1,000 (10-20x risk in general population)
  - Apical displacement of posterior and septal tricuspid valve leaflets, atrialization of right ventricle, +/− ASD or patent foramen ovale
- 3rd trimester use controversial:
  - Some studies show association with:
    - Hypothyroidism
    - Floppy baby syndrome
    - Premature delivery
- Restriction in labor controversial
  - Restart when pt is medically stable postpartum, using preconception dose
  - Incr risk of lithium toxicity following delivery d/t large volume loss
- Restriction in breastfeeding controversial
  - Recent study showed average breastfed infant serum lithium level = 0.16meq/L, and no adverse effects noted in infants
- Therapeutic serum level: 0.8-1.2 meq/L
- Toxicity at serum level ≥1.5 meq/L
  - Vertigo
  - Sedation
  - Arousal
  - Coarse hand tremor
  - Muscle weakness
  - Cardiac arrhythmias
- Serum levels >2.5 meq/L
  - Coma
  - Renal failure
  - Seizures
  - Death
  - Valproate
    - Pregnancy Category D
    - Avoid during pregnancy
    - Spina bifida risk 1-5% (15-30 day post-fertilization)
    - Craniofacial and cardiac defects, polydactyly, hypospadias, low birthweight
    - SE: nausea, blurred vision, nystagmus, sedation, vertigo
    - Rarely: agranulocytosis, aplastic anemia
    - 4 mg Folic acid supplement recommended
  - Carbamazepine
    - Pregnancy Category D
    - Spina bifida risk 0.5-1.0% (15-30 day post-fertilization)
    - Meningomyelocele, anal atresia, ambiguous genitalia, cardiac defects, craniofacial abnormalities, torticollis
    - 4 mg folic acid supplement recommended
    - Additional 20 mg of vitamin K supplement daily at 36 wks until delivery
Follow-Up
1. Return to office if pt experiences:
   - Depression
   - Agitation
   - Manic symptoms
2. Time frame for return visit
   - Follow-up for eval of psychiatric status within first 2 wks postpartum
3. Refer to specialist
   - Women w/bipolar disorder should be referred to a psychiatric professional for eval and tx
   - Psychiatric consult ideal during hospitalization for delivery
4. Admit to hospital
   - Acute manic event/ relapse
   - Suicide/ homicide risk
     - Suicidal/ homicidal ideation/ intent/ plans
     - Access to means for suicide
     - Command hallucinations, other psychotic symptoms or severe anxiety
     - Alcohol or substance use
     - Hx of previous attempts
     - Family hx of or recent exposure to suicide

Prevention
1. Effective contraception for all female pts receiving drug tx for bipolar disorder
   - Carbamazepine, oxcarbazepine, and topiramate incr metabolism of OCPs
   - Do not rely on OCPs alone
2. Pregnancy should be planned in consultation w/psychiatrist

References

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